UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/852,845	05/11/2001	Wayne Godfrey	16524.010	7084

28381 7590 09/23/2003

ARNOLD & PORTER
IP DOCKETING DEPARTMENT; RM 1126(b)
555 12TH STREET, N.W.
WASHINGTON, DC 20004-1206

EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	17

DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/852,845	GODFREY ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06/27/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *83,84,86,88-90 and 92-119* is/are pending in the application.

4a) Of the above claim(s) *100-115* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *83,84,86,88-90,92-99 and 116-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/30/03 has been entered.

Claims 83-84, 86, 88-90 and 92-119 are pending.

2. Newly submitted claims 100-108 and 109-115 directed to an inventions that are independent or distinct from the invention originally claimed for the following reasons: The invention of the elected group I, claims 35, 59-72 and 78-91, now claims 83,84, 86, 88-90, 92-99 and 116-119 are drawn to a monoclonal antibody that specifically binds to an ACT-4-h –1 receptor polypeptide and is generated by hybridoma HBL106, humanized antibody or fragment thereof, which binds to an ACT-4-h-1, wherein humanized heavy and light chains comprises three complementarity determining regions and wherein said antibody competes with a monoclonal antibody generated by hybridoma HBL106, an antibody and monoclonal antibody which specifically binds an ACT-4-h-1 receptor and competes with a monoclonal antibody generated by hybridoma HBL106 . The invention of newly added claims 100-108 is related to a an antibody that does not compete with the monoclonal antibody generated by hybridoma HBL106. The invention of newly added claims 109-115 is related to an anti-idiotypic antibody.
Antibody that competes with a monoclonal antibody generated by hybridoma HBL106 and antibody that does not competes with a monoclonal antibody generated by hybridoma HBL106 and an anti-idiotypic antibody differ with respect to their structures, specific binding epitopes, and physicochemical properties; therefore each product is patentably distinct.

Claims 100-115 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 83, 84, 86, 88-90, 92-99 and 116-119 drawn to humanized antibody or fragment thereof, which binds to an ACT-4-h-1, wherein humanized heavy and light chains comprises three complementarity determining regions and wherein said antibody competes with a monoclonal antibody generated by hybridoma HBL106, an antibody and monoclonal antibody which specifically binds an ACT-4-h-1 receptor and competes with a monoclonal antibody generated by hybridoma HBL106 under consideration in the instant application.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 84, 88, 90, 92-99 and 118 -119 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention essentially for the same reasons set forth in the previous Office Action, paper NO:10, mailed 12/31/02.

5. It is apparent that L 106 antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the pertinent cell lines which produce these antibodies. See 37 CFR 1.801-1.809.

Applicant's arguments, filed 5/30/03 , Paper No. 12 have been fully considered, but have not been found convincing.

Applicant filed a Deposit Declaration with an attached copy of the Receipt of an Original Deposit indicating that hybridoma cell line L106 has been made under the terms of the Budapest Treaty.

In addition to the conditions under the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridoma cell line L106 has been deposited under the Budapest Treaty and that the hybridoma cell line L106 will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or for the enforceable life of the patent whichever is longer. See 37 CFR 1.806., 1.808 (a)(2) and MPEP 2410-2410.01

6. Claims 83, 84, 86, 88-90, 116, 117 and 119 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection.**

7. A humanized antibody wherein humanized heavy chain comprises at least one of the complementary determining regions, claimed in 83 and 89; a humanized antibody wherein humanized light chain comprises at least one of the complementary determining regions, claimed in 84 and 89; an antibody or fragment thereof wherein said antibody specifically binds an ACT-4-h-1 receptor and may be produced by immunizing an animal with purified ACT-4 receptor polypeptide or with ACT-4-h-1 receptor polypeptide, claimed in claims 116 and 117; a monoclonal antibody wherein said monoclonal antibody specifically binds to an ACT-4-h-1 receptor, competes with a monoclonal antibody generated by hybridoma HBL106 and is fused to a coat protein of a filamentous phage, claimed in claim 119 represent a departure from the specification and the claims as originally filed and applicant has not pointed out where the support come from. The specification and the claims as originally field only support a humanized antibody wherein humanized heavy chain comprises three complementary determining regions and wherein humanized light chain comprises three complementary determining regions. The specification and the claims as originally field does not support an antibody or fragment thereof wherein said antibody specifically binds an ACT-4-h-1 receptor and may be produced by immunizing an animal with purified ACT-4 receptor polypeptide or with ACT-4-h-1 receptor polypeptide, claimed in claims 116 and 117; a monoclonal antibody wherein said monoclonal antibody specifically binds to an ACT-4-h-1 receptor, competes with a monoclonal antibody generated by hybridoma HBL106 and is fused to a coat protein of a filamentous phage, claimed in claim 119.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 83, 84, 86, 88-90, 92-99 and 116-119 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention essentially for the same reasons set forth in the previous Office Action, paper NO:10, mailed 12/31/02.

Applicant is in possession of: humanized antibody or fragment thereof, which binds to an ACT-4-h-1 of SEQ ID NO:2, wherein humanized heavy and light chains comprises three complementarity determining regions and wherein said antibody competes with a monoclonal antibody generated by hybridoma HBL106, an antibody and monoclonal antibody which specifically binds an ACT-4-h-1 receptor of SEQ ID NO:2 and competes with a monoclonal antibody generated by hybridoma HBL106

Applicant is not in possession of : humanized antibody or fragment thereof, which binds to *any* ACT-4-h-1 receptor, wherein humanized heavy and light chains comprises three complementarity determining regions and wherein said antibody competes with a monoclonal antibody generated by hybridoma HBL106, an antibody and monoclonal antibody which specifically binds *any* ACT-4-h-1 receptor and competes with a monoclonal antibody generated by hybridoma HBL106

Applicant asserts that amended claims read on antibodies or antibody fragments that specifically binds an ACT-4-h-1 receptor that is fully described.

Contrary to Applicant's assertion, the specification fails to described *any* ACT-4-h-1 receptor. Applicant has disclosed only one ACT-4-h-1 receptor of SEQ ID NO:2 ; therefore, the skilled artisan cannot envision all the contemplated antibody possibilities broadly recited in the instant claims. In addition, the Specification disclosed that 50 kDa polypeptide is refers as ACT-4-h-1 receptor. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of antibody may be achieved by means of a recitation of a representative number of antibody, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 83, 84, 86, 88-90 and 116-119 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No 6,277,962 .

Although the conflicting claims are not identical, they are not patentably distinct from each other because US Patent 6,277,962 teaches an antibody, a monoclonal antibody, a fragment of said antibody that specifically binds to an ACT-4-h-1 receptor and competes with an antibody generated by hybridoma HBL106, wherein said antibody is fused to a coat protein of a filamentous phage a monoclonal antibody that specifically binds to an ACT-4-h-1 receptor polypeptide, wherein said antibody is fused to a coat protein of a filamentous phage, an immunotoxin comprising said antibody fused to a toxin polypeptide, a monoclonal antibody for specific binding to a ACT-4-h-1 receptor polypeptide and specifically binds to a different epitope on said receptor than that specifically bound by antibody generated by hybridoma HBL106 (see claims 1-13). US Patent 6,277,962 teaches generation of a humanized antibody by linking the CDR regions of a non-human antibodies to human constant regions wherein humanized heavy and light chains comprises three complementarity determining regions. US Patent 6,277,962 teaches that said antibody would have different binding specificity and affinity than antibody generated by hybridoma HBL106 (see column 15, lines 13-65 and column 16, lines 53-60 in particular). US Patent 6,277,962 teaches that said antibody have a capacity to stimulate or inhibit activation of CD4+ cells (see column 16, lines 60-65 in particular) US Patent 6,277,962 teaches an antibody that specifically binds an ACT-4-h-1 receptor can be produced by immunizing an animal (see column 15, lines 14-25 in particular) .

12. Claims 92-99 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No 6,277,962 in view of Owens *et al* (J.of Immunol.. Method. 1994) and Bird *et al* (Science,1988).

The teaching of US Patent 6,277,962 has been discussed, supra

The claimed invention differs from the US Patent 6,277,962 teaching only by the recitation of an antibody or fragment thereof that specifically binds an ACT-4-1 receptor and has different binding specificity than antibody generated by hybridoma HBL106 ,antibody, Fab fragment of said antibody, Fab' fragment of said antibody, $F(ab')_2$ fragment of said antibody, Fabc fragment of said antibody, Fv fragment of said antibody.

Owens *et al* teach the modification of murine antibodies such as a chimeric antibody, a single chain antibody, a Fab fragment, a $F(ab')_2$ fragment or a humanized antibody , monoclonal antibody technology including, chimeric, single chain, Fab fragments, and $F(ab')_2$. Owens *et al* further teach humanized antibodies use in therapy of human diseases or disorders, since the human or humanized antibodies are much less likely to induce an immune response. Also, antibody fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement - dependent cytotoxcity (see the entire document).

Bird *et al* teach a single chain antigen binding proteins composed of an antibody variable light - chain amino acid sequence (V_L) tethered to a variable heavy -chain sequence (V_H) by a designed peptide that links the carboxyle terminus of the V_L sequence to the amino terminus of the V_H sequence. Bird *et al* further teach that the single chain antibodies have significant advantages over monoclonal antibodies in a number of applications such as lower back ground in imaging applications since the single chain antibody lack the Fc portion (see the entire document and page 426, left column, 2nd paragraph in particlular)).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use antibody taught US Patent 6,277,962 to make antibody or fragment thereof that specifically binds an ACT-4-1 receptor and has different binding specificity than antibody generated by hybridoma HBL106 , antibody, Fab fragment of said antibody, Fab' fragment of said antibody, $F(ab')_2$ fragment of said antibody, Fabc fragment of said antibody, Fv fragment of said antibody taught by Owens *et al.* or as a single chain antibody as taught by the Bird *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al.* and because single chain antibodies have significant advantages over monoclonal antibodies in a number of applications

such as lower back ground in imaging applications since the single chain antibody lack the Fc portion as taught by Bird *et al.*

11. Claims 116 and 117 are rejected under 35 U.S.C.102(b) as being anticipated by Knapp et al. (Leucocyte Typing IV,1989) essentially for the same reasons set forth in the previous Office Action, paper NO:11, mailed 12/31/02.

Knapp et al. teach the L106 antibody (Table 4, page 391, or Table 1, page 482 in particular).

Applicant's arguments, filed 5/30/03 , Paper No. 12 have been fully considered, but have not been found convincing.

Applicant asserts that the Knapp et al., is silent with regard to antibody that specifically binds ACT-4 receptor. However, Knapp et al., teach the same antibody as claimed antibody generated by hybridoma HBL106, that will inherently specifically binds to ACT-4 receptor.

Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not bind to ACT-4-h-1 or ACT-4 as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980). In addition, applicant is invited to consider the following decisions based upon generating antibodies. Whether the rejection is based on "inherence" under 35 U.S.C. § 102 or prima facie obviousness under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. Examiner properly shifted burden to applicant to establish, through objective evidence, that hybridoma and monoclonal antibody of invention differ in unobvious manner from those of the prior art references. Ex parte Phillips, 28 USPQ2d 1302 (BPAI 1993).

Moreover, a recitation of the intended use of the claimed invention (that is the ability of L106 antibody to bind to ACT-4-h-1) must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. For example in Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); the following was noted. "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

13. Claim 119 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knapp et al. (Leucocyte Typing IV,1989) in view US Patent 6,277,962

The teaching of Knapp et al. has been discussed supra.

The claimed invention differs from the Knapp et al. reference teaching only by the recitation of a monoclonal antibody that specifically binds to an ACT-4 receptor and is fused to a coat protein of a filamentous phage .

US Patent '962 teaches a monoclonal antibody that is fused to a coat protein of a filamentous phage (see entire document, Claim 6 in particular). US Patent '962 teaches that said antibody can be used to specifically target activated cells (see column 7 in particular).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to generate antibody taught by US Patent '962 using the antibody taught by Knapp et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the antibody could be used to specifically target cells as taught by US Patent '962.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
September 22, 2003

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600